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Muttenz, 21st of April 2005

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450
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With regard to:

- **US Patent Application 10/711,389 (Filing Date 09/15/2004)**
- **Fax 7th of April 2005**
- **Fax 21st of April 2005**

Dear Sir or Madam

As I wrote to you, I did not know before 1st of April 2005 that somebody had applied for a US patent on 15th of September 2004 although I am first named inventor of prior CH-01833/03.

Yesterday I signed the corresponding DECLARATION FOR UTILITY OR DESIGN PATENT APPLICATION (first named inventor: Werner Zumbrunn) after having reviewed the application.

I have not been involved in preparing the application and was not allowed to make any contribution to the description and the claims. Therefore I do not agree with everything. I disclosed my review to another joint inventor but he does not accept my considerations.

Therefore I hereby disclose parts of my review to the USPTO.

Summary of the invention

[Para 19]: US587322 doesn't exist. Perhaps US5879322 is meant?

[Para 28, first sentence]: It is mentioned that "an active substance (drug) normally is dissolved in a fluid solution comprising a solvent." Therefore it is incomprehensible when the next sentence reads as follows: "The active substance or the solvent are dispensed directly or indirectly (...)."

[Para 34, 37 and others]: Throughout the description sentences as follows are used: "The solvent recovery means serve to remove **depleted** solvent from the interface (...)." In a lot of cases the fluid solution is not depleted but the concentration of the

drug in the fluid solution rises. In these cases the above mentioned description is wrong.

[Para 34, 37]: The sentences "e.g. after repeated dispensing, active substance concentration maintains at a certain concentration and no unwanted substance is accumulated within the device" or "The solvent recovery element serves the purpose of removing **depleted** solvent from the interface so that, after repeated dispensing, drug concentration maintains its highest value and no freely moving liquid is formed within the device" are not correct.
There are three different cases depending on the permeation rate of the active substance through the skin in relation to the permeation rate of the solvent into the recovery element. Perhaps the authors of the patent description regarded this topic as to be too complicated to be mentioned.

[Para 39]: The sentence "By this it is possible to avoid **negative decrease** of the active substance due to accumulation of the solvent which would impact the diffusion rate through the skin" is not correct.
The active substance does not decrease due to accumulation of the solvent but the **concentration of the active substance** can decrease in this case.

[Para 46/Line 1 to 16, corresponding to figure 4 a) and 4 c) of the drawings]: This first embodiment of a solvent removal system cannot work: When the fluid solution is distributed all over the interface device 12 the solvent cannot be reclaimed by a micro pump or tubing filled with absorbent material. It is impossible because of physics.

[Para 46/Line 16 to 23]: This second embodiment of a solvent removal system has the disadvantage that not only the solvent is picked up but also the dissolved drug. Apart from that the "invention" is obvious if one knows CH-01833/03 the priority of which is claimed.

[Para 46/Line 23 to 30]: This third embodiment of a solvent removal system corresponds to an embodiment in CH-01833/03.

[Para 46 Line 30 to 36]: This forth embodiment of a solvent removal system is not comprehensible to me; I think it is also not comprehensible to a person having ordinary skill in the art. What is a "timed capillary action of a sponge?"

[Para 47]: The explanation why the modulated dispensing of drug formula brings about a significant increase of delivery rate is not correct. Three different cases have to be taken into account (see discussion of Para 34, 37).

[Para 50]: As already mentioned in the discussion of Para 46/first embodiment, "solvent removal means with a desiccant/absorbent connected to the interface by a tube, a desiccant/absorbent connected to the interface by a tube which compromises a valve" cannot function because of physics.

[Para 57 to 65/Figure 1]: This first embodiment corresponds more or less to an embodiment in CH-01833/03.

[Para 65, last line]: "Thereby the **concentration of the dissolver** in the region of the interface 12 may be kept below a certain level." This explanation is not correct. The

dissolver itself has not "a concentration". Therefore it cannot be kept "below a certain level."

[Para 66 to 67/Figure 2]: This further (second) embodiment corresponds more or less to an embodiment in CH-01833/03.

[Para 68 to 71/Figure 3]: This third embodiment corresponds more or less to an embodiment in CH-01833/03 with the exception that now two drug reservoirs are provided.

[Para 68/Line 6 and 21 and Para 71/Line 12]: Control device 15 is wrong. Control device 8 is probably correct.

[Para 72 to 75/Figures 4 a) to 4 c)]: These three further embodiments are characterized by two things:

- In two embodiments a waste pipe 41 is provided.
- If administration of the active substance needs to be stopped it is possible to pump active substance from the administration chamber back into the ~~administration~~ **drug** reservoir 5 or the connecting pipe 4 by pump 36.

Pumping back of active substance into the drug reservoir is not subject matter of the prior invention. The removal of the "depleted solvent" by a second valve 37 and waste pipe 41 instead of the above mentioned means for removal of solvent could be a new invention of a joint inventor unknown to me. Unfortunately, because of physics, it is impossible to remove "the depleted solvent" by pumping or sucking because the active substance/fluid solution is distributed all over the interface 12 and cannot be reclaimed by pumping or sucking (see also discussion of paragraph 46).
The pumping back or sucking of solvent is only partially possible if the administration chamber 9 is filled with active substance, i.e. a good deal more of "active substance" is dispensed than can be accepted by the interface 12. Because the "active substance" absorbed by the interface cannot be removed by pumping or sucking this invention makes no sense.
Only embodiment 4 b) makes sense concerning the removal of solvent. Unfortunately it is not obvious how the removal of solvent should be managed.

Claims

[Claim 1]: There is an incompatibility between step b) and c) and therefore these steps are not comprehensible:
In b) is stated that the solvent is removed in order **to achieve a certain level** of concentration in vicinity to a porous surface to be treated.
In c) is stated that there is absorption of active substance by the surface to be treated such that **the level of concentration in the administration reservoir decreases**.

The problem is that there aren't two steps or sequential processes but these two processes are **concurrent**. What happens after "dispensing a certain amount of a liquid" depends on the permeation rate of the drug through the skin in relation to the permeation rate of the solvent into the recovery element (see discussion of paragraph 34, 37).

[Claims 5 and dependent claims 6 and 9]: Impossible because of physics (as mentioned above).

[Claims 10 and 11]: I think there must be a mistake: "(...) one of the claims 2 wherein (...)"?

[Claim 17, line 8]: The removal of the solvent cannot only happen by evaporation but by diffusion, too.

Drawings

[Fig. 3]: The reference character 25 appears twice.
[Fig. 4c)]: The reference character 37 (valve and/or micro pump) is missing. The reference character 41 points to the wrong object.

With kind regards,

Werner Zumbrunn